

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

FY 2002 Hearing on Chronic Diseases

**Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations**

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National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)**

March 28, 2001

Mr. Chairman and Members of the Committee: I am pleased to testify on behalf of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which supports research on a wide range of chronic, debilitating diseases including diabetes, hepatitis and other chronic liver diseases, inflammatory bowel disease, interstitial cystitis and other chronic bladder conditions, chronic prostatitis, chronic anemias, polycystic kidney disease, and end stage kidney disease. The economic burden of these diseases accounts for a major proportion of U.S. health care expenditures. According to a recent study conducted on behalf of the Johns Hopkins University and the Robert Wood Johnson Foundation, 125 million Americans suffer from at least one chronic condition, and 60 million live with multiple chronic conditions. The study predicts that half of the U.S. population will suffer from chronic conditions by 2020, consuming 80 percent of health care spending. Advances in biomedical research are critical if we are to mitigate the human and economic burden of chronic diseases. With the increased funding Congress has provided, NIDDK-supported scientists are well positioned to identify the causes of the chronic diseases within our mission, to help identify people at risk for development of these diseases, and ultimately, to provide novel approaches to prevention and treatment.

DIABETES

One of the most important health care issues facing our Nation is the burden of diabetes. According to the Centers for Disease Control and Prevention (CDC), diabetes affects an estimated 16 million Americans, one-third of whom are unaware they have the disease. An estimated 30 million additional Americans have a pre-diabetic condition termed impaired glucose tolerance. Within the last year, scientists have made tremendous progress in understanding and treating both type 1 and type 2 diabetes. Type 1, or juvenile diabetes, occurs when the body's immune system destroys the insulin-producing beta cells in the islets of the pancreas. Although typically diagnosed in children and adolescents, it can occur at any age. Type 2 diabetes, previously called non-insulin dependent or adult-onset diabetes, results from the body's inability to

respond to insulin effectively—a condition known as insulin resistance—followed by a failure of the pancreatic islets to produce sufficient insulin.

Recent advances have created new hope for using pancreatic islet transplantation to cure type 1 diabetes. The NIDDK is funding several clinical trials to expand upon a promising pilot protocol that has enabled a number of people with type 1 diabetes to remain healthy for over a year after receiving islet transplants, without receiving insulin injections. We are supporting research on every aspect of islet beta cell development and function so that we can address problems with inadequate supplies of donor pancreatic tissue for transplantation by developing alternative sources of islet beta cells. In addition, we are supporting research on alternatives to lifelong immunosuppressive drug treatment to prevent rejection of transplanted islets. One innovative approach teaches the immune system to accept a transplant as “self,” thus avoiding tissue rejection without global immunosuppression. Not only do these promising techniques increase the likelihood of achieving a true cure for type 1 diabetes, but they also offer hope of intervening early in those at risk to prevent type 1 diabetes. Pilot trials of innovative prevention measures will be performed in our newly-created type 1 diabetes Trial Network.

Obesity is a major risk factor for type 2 diabetes. The alarming increase in the number of people who are overweight or obese in the U.S. population has led to an increasing incidence of type 2 diabetes in adults, and even in children and adolescents. Recent studies have identified links between proteins produced by fat cells and type 2 diabetes. An increased number of fat cells—as seen in overweight or obese patients—causes an increase in levels of these proteins. For example, NIDDK grantees identified a gene they termed “resistin” that codes for a hormone produced by fat cells. In mouse models, both genetic and diet-induced obesity were associated with elevated levels of resistin in the blood. Resistin was so named because it causes insulin resistance; blocking the action of resistin in a diabetic mouse model eliminates insulin

resistance and improves disposal of blood sugar. Currently, investigators are extending their studies on this novel gene to humans. Drugs that block resistin action may prove useful in both treatment and prevention of type 2 diabetes.

This is but one example of NIDDK-supported efforts to mine the human and mouse genome sequences with the goal of identifying genes involved in susceptibility to diabetes. In most people, more than one genetic alteration or mutation is necessary for development of type 2 diabetes. Researchers have already identified several genes that may play a role in this disease. The gene *NIDDM1* was identified in a group of Mexican Americans known to be particularly prone to type 2 diabetes. The product of this gene, calpain 10, is an enzyme present in tissues—such as pancreatic islets, muscle, and liver—that are involved in insulin and glucose processing. Scientists have identified at least three other chromosomal regions that may interact to cause susceptibility to type 2 diabetes. Knowledge of the genetic basis for diabetes susceptibility paves the way to improved prevention, diagnosis, and treatment.

In addition to genetic susceptibility, the environment plays a major role in development of type 2 diabetes. For this reason, the NIDDK is supporting an initiative on new environmental approaches to obesity prevention. We are also launching a major initiative aimed at prevention and treatment of type 2 diabetes in children and adolescents. We are increasing the resources available to our Diabetes Research and Training Centers so that they can enhance their efforts on diabetes prevention and treatment. We are expanding the efforts of our National Diabetes Education Program, which supports community-based multi-cultural efforts to increase diabetes awareness. Our major multi-center clinical trial, the Diabetes Prevention Program, is testing the ability of lifestyle and drug intervention strategies to prevent type 2 diabetes in individuals with impaired glucose tolerance who are at high risk for the disease. A positive outcome to this trial, whose completion is expected in 2002, would have major public health implications.

Many devastating complications accompany both type 1 and type 2 diabetes. Diabetes is the leading cause of end stage kidney disease, new cases of blindness in adults, and non-traumatic lower limb amputations. It also causes increased susceptibility to urinary tract infections, poorly healing skin ulcers, periodontal disease, and a non-alcohol-related progressive form of fatty liver disease known as NASH. Heart disease is the leading cause of death in diabetics. Because the complications of diabetes affect so many organ systems, the NIDDK has developed productive collaborations with many of the Institutes represented on this panel, as well as with other Institutes and Centers. Together, we are exploring all avenues of prevention and treatment for the complications of diabetes, including basic genetic and molecular studies, development of animal models to facilitate testing of new drugs, therapeutic gene transfer techniques, and drug intervention.

HEPATITIS C

The NIDDK also funds research into many other serious chronic diseases. In the U.S., hepatitis C infection is the leading cause of liver failure. The newly-initiated HALT-C trial is testing whether long-term antiviral treatment can eliminate the hepatitis C virus in patients who fail to respond to conventional treatment, and thereby prevent the long term consequences of hepatitis C infection: liver failure and liver cancer. We are also initiating a trial of interferon treatment of hepatitis C in African Americans who are often more resistant to treatment.

INFLAMMATORY BOWEL DISEASE

We are sponsoring studies into the mechanisms underlying inflammatory bowel disease (IBD)--ulcerative colitis and Crohn's disease--including identification of genetic and environmental causes. Previous work on inflammatory signals led to development of a treatment effective in many patients with Crohn's disease. The

NIDDK plans to sponsor an IBD Genetics Consortium and form a clinical network to accelerate studies of IBD.

END STAGE KIDNEY DISEASE AND POLYCYSTIC KIDNEY DISEASE

According to the U.S. Renal Data System, individuals with diabetes account for approximately 45 percent of patients with end stage kidney disease. Because of this, we are concentrating our efforts on preventing and slowing the progression of diabetic kidney disease. NIDDK funding is also making a difference in understanding other important causes of irreversible kidney failure such as polycystic kidney disease (PKD). In addition to work on the genes responsible for causing PKD, NIDDK-funded researchers are developing a non-invasive means of assessing PKD progression, which will facilitate planned clinical testing of drug and other interventions. A new observational study is aimed at understanding the factors responsible for the high incidence of heart disease in patients with end stage kidney disease. We are also launching a National Kidney Disease Education Program to address the rising incidence of end stage kidney disease, particularly in various minority groups.

UROLOGIC DISEASES

The NIDDK is also sponsoring initiatives to promote understanding of urologic diseases, including interstitial cystitis, benign prostatic hyperplasia, and chronic prostatitis. Epidemiologic efforts, clinical trials, research networks, and laboratory studies are leading to improved diagnosis and treatment for these diseases as well.

The NIDDK will continue to do everything within its means to combat the many serious chronic diseases within its mission in order to relieve the burden they place on individuals, families, and the Nation. I appreciate the opportunity to address the Committee, and I thank you for your attention.

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National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases

Biographical Sketch

NAME : Allen M. Spiegel, M.D.

POSITION : Director, National Institute of Diabetes and Digestive and Kidney Diseases

BIRTHPLACE : Germany

DATE: May 18, 1946

EDUCATION : B.A., Columbia College, 1967
M.D., Harvard Medical School, 1971

EXPERIENCE

1999-present : Director, National Institute of Diabetes and Digestive and Kidney Diseases, NIH

1990-1999 : Director, Division of Intramural Research, National Institute of Diabetes and Digestive and Kidney Diseases, NIH

1993-present : Chief, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH

1988-1993 : Chief, Molecular Pathophysiology Branch, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH

1985-1988 : Chief, Section on Molecular Pathophysiology, Metabolic Diseases Branch, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, NIH

1977-1984 : Senior Investigator, Metabolic Diseases Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH

- 1973-1976 : Fellow, NIH Endocrinology Training Program, Clinical Associate, Metabolic Diseases Branch (Dr. G. D. Aurbach, Chief), National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH
- 1971-1973 : Intern and Assistant Resident in Medicine, Massachusetts General Hospital, (Dr. Alexander Leaf, Chief)

**HONORS AND
AWARDS**

- 1966 - Elected to Phi Beta Kappa
1967 - B.A. Summa Cum Laude
1971 - Elected to Alpha Omega Alpha
1971 - M.D. Cum Laude
1988 - Outstanding Service Medal – U.S. Public Health Service
1990 - Meritorious Service Medal – U.S. Public Health Service
1990 - Jacobaeus Prize – Nordisk Insulin Foundation
1993 - Plenary Lecturer – Japan Endocrine Society
1993 - Aurbach Memorial Lecturer – American Society for Bone and Mineral Research
1994 – Harrison Memorial Lecturer – Endocrine Society of Australia
1996 - Komrower Memorial Lecturer – Society for the Study of Inborn Errors of Metabolism
1998 - Edwin B. Astwood Lecture Award – Endocrine Society (U.S.A.)

**PROFESSIONAL
ORGANIZATIONS**

American Federation for Clinical Research
The Endocrine Society
American Society for Bone and Mineral Research
American Society for Clinical Investigation
American Society for Biochemistry and Molecular Biology
Association of American Physicians

**LICENSURE AND
CERTIFICATION:**

Diplomate American Board of Internal Medicine, 1974
Board Certified in Endocrinology, 1975
Licensed in Medicine, Maryland